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A multicentre audit of outpatient care for adult anorexia nervosa: Symptom trajectory, service use, and evidence in support “early stage” versus “severe and enduring” classification.

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1 Partnership NHS Foundation Trust, Worcestershire Health and Care NHS Trust. We are grateful  
2 to all our study participants for their patience and perseverance.

3 **Data availability**

4 The authors had full access to the trial data and continue to do so. The deidentified study  
5 data will be made publicly available by December 2020.

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7

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## Abstract

**Background:** We explored the clinical utility of “staging” anorexia nervosa (AN) based on duration of illness and psychological wellbeing. We also investigated 12-month symptom trajectories and service usage in a large cohort of patients with AN assessed for outpatient treatment. **Method:** We conducted secondary analyses on data from a multisite clinical trial of adults with AN ( $N=187$ ) recruited from 22 NHS England specialist eating disorder outpatient services into a digital treatment augmentation study. Clinical outcomes and service use were measured at post-intervention (six weeks), 6 and 12 months. We grouped patients into two categories: “early stage” (illness duration  $<3$  years;  $n=60$ ) and “severe and enduring” stage (SE-AN;  $n=41$ ) indicated by distress (Depression Anxiety and Stress Scales, DASS  $\geq 60$ ) and illness duration ( $\geq 7$  years). **Results:** Overall, patients reported large to moderate improvements from baseline to 12 months in body mass index, eating disorder symptoms, and moderate improvements in mood and work/social adjustment, and 23.6% met criteria for recovery. However, patients classified as SE-AN reported higher rates of accessing intensive services, higher eating disorder symptomatology, and poorer work/social adjustment at baseline, and lower rates of improvement in work/social adjustment at 12 months compared to “early stage” respondents. **Discussion:** Although present findings suggest overall symptomatic improvements, exploratory results highlight marked differences in course and service use between people at different stages of AN and suggest a need to consider staging for clinical decision-making. Treatment research differentiating between clinical subtypes of AN and adoption of a more personalized approach may ensure that services and care pathways better fit patient needs.

**Keywords.** Anorexia nervosa, classification, staging, outpatient care, treatment outcomes, illness duration, social adjustment.

1           **Trial Registration number:** ISRCTN ClinicalTrials.gov NCT02336841

2

1 A multicentre audit of outpatient care for adult anorexia nervosa: Symptom trajectory, service  
2 use, and evidence in support “early stage” versus “severe and enduring” classification.

3 Anorexia nervosa is a debilitating illness that often runs a chronic course and is  
4 associated with increased mortality rates, substantial physical and psychological comorbidities,  
5 and adverse social consequences (Arcelus, Mitchell, Wales, & Nielsen, 2011). Many patients  
6 gradually recover, but longitudinal studies indicate that 61% of people with anorexia nervosa  
7 continue to exhibit illness symptoms at 5-year follow-up (Støving, Andries, Brixen, Bilenberg, &  
8 Hørder, 2011), and nearly 40% of remain ill at 22-year follow-up (Eddy et al., 2017). Recent  
9 findings suggest that although interventions generally yield small improvements in body weight  
10 (with greater effects for specialized treatments over comparator treatments), these effects are not  
11 maintained at follow-up, and treatment effects on psychological functioning are nonsignificant  
12 (Murray, Quintana, Loeb, Griffiths, & Le Grange, 2018); thus, clinical outcomes seem to vary by  
13 the nature of the assessment variable and timing of assessment. Indeed, treatment outcome  
14 research for AN is frequently challenged by relatively short follow-up periods, small sample  
15 sizes, and limited ecological validity given the highly controlled nature of most clinical trials.  
16 Other difficulties include differences in inclusion criteria (e.g., whether or not a minimum BMI  
17 cut-off is used), differences in reporting and access to rescue treatment (e.g., the numbers who  
18 are admitted to higher levels of care), differences in protocols for those who receive higher levels  
19 of care, as well as differences in outcome measures (e.g., BMI versus psychosocial functioning).  
20 Moreover, there is disagreement among experts regarding the salience (and characteristics) of  
21 illness severity and chronicity for treatment outcomes: whereas some highlight the clinical  
22 impacts of neuroprogression (Treasure, Stein, & Maguire, 2015), others posit that “severe and  
23 enduring” classification schemes have little clinical utility (Raykos, Erceg-Hurn, McEvoy,

1 Fursland, & Waller, 2018). These controversies underscore the need to better understand the  
2 trajectory of illness, use of services, and roles of illness duration and severity among individuals  
3 receiving treatment for adult anorexia nervosa.

4       Although patients advocate for more research to understand the processes of symptom  
5 duration and recovery (van Furth, van der Meer, & Cowan, 2016), there are many uncertainties  
6 related to planning appropriate care pathways for adult anorexia nervosa (NHS England, 2019;  
7 NICE, 2017). Research suggests that early interventions produce good outcomes (McClelland et  
8 al., 2018) whereas people with an enduring form of illness respond less well (Russell, Szmukler,  
9 Dare, & Eisler, 1987) and longer duration predicts poorer eating disorder outcomes (Fichter,  
10 Quadflieg, & Hedlund, 2006). These findings suggest that a staging model may be applicable to  
11 anorexia nervosa (Treasure et al., 2015). However, there is currently no accepted marker of  
12 disease progression or clinical features that might be used to stage the illness (Wonderlich et al.,  
13 2012). Following Russell's lead it has been common to define the "early stage" of illness as less  
14 than 3 years in duration (Treasure et al., 2015), a classification scheme that has demonstrated  
15 some clinical utility. For instance, research suggests that in adolescence those in the early stage  
16 responded well to family based therapy (Russell et al., 1987). More recently it has been found  
17 that a tailored intervention for those in the early stage of illness improves outcome (Fukutomi et  
18 al., 2019; McClelland et al., 2018) and this has been cited as an example of good practice in a  
19 recent UK Commissioning report (NHS England, 2019).

20       There is less consensus in the field regarding the definition of later stages of illness in  
21 anorexia nervosa. Terms such as "severe and enduring" anorexia nervosa (SE-AN), "chronic,"  
22 "persistent," and "treatment-resistant" have been used to describe those who have been ill for a  
23 longer period of time (Broomfield, Stedal, Touyz, & Rhodes, 2017). Notably, severity and



1 duration of illness appear to represent distinct dimensions, suggesting that reliance solely on the  
2 “enduringness” component would be insufficient (Coutinho & Brandão, 2019; Wildes et al.,  
3 2017). A modal cut-off of 7 years is commonly employed to describe “long” illness duration and  
4 markers of severity including body mass index and number of treatment attempts have been  
5 proposed but not received consensus (see (Broomfield et al., 2017) for a review). For instance,  
6 body mass index is used as a marker of severity in DSM-5 but several studies have questioned  
7 this proposal (Machado, Grilo, & Crosby, 2017; Smith et al., 2017). Instead, patients identified  
8 as having severe and persistent forms of illness have highlighted negative mood and poorer  
9 social functioning as core illness markers (Arkell & Robinson, 2008), suggesting that these may  
10 be valuable indicators of chronicity in anorexia nervosa. Indeed, patients and carers prioritise  
11 social function and mood as relevant treatment outcomes (Himmerich et al., 2018; Linville,  
12 Brown, Sturm, & McDougal, 2012; Pettersen & Rosenvinge, 2002). Moreover, emotional  
13 distress is well-established as an underlying maintenance factor for eating disorders (Schmidt &  
14 Treasure, 2006; Treasure & Schmidt, 2013). For example, a network analysis found that  
15 depression, anxiety and interpersonal sensitivity were nodes with the highest centrality in the  
16 network of symptoms in AN (Solmi, Collantoni, Meneguzzo, Tenconi, & Favaro, 2019). Another  
17 network analysis from a large population of adolescents with anorexia nervosa found that  
18 depressive symptoms and personal alienation were central features that played a key bridging  
19 role (Monteleone et al., 2019). Treatment studies also support the centrality of mood in AN: for  
20 instance, proof of concept studies testing neuromodulation interventions used for treatment  
21 resistance in depression and obsessive-compulsive disorder have shown some promise with an  
22 improvement in mood as the main initial effect, albeit with mixed impact on AN  
23 symptomatology (Dalton et al., 2018; Lipsman et al., 2017; McClelland, Kekic, Campbell, &

Schmidt, 2016). Mood-related symptoms may also offer prognostic utility in AN: one longitudinal study of eating disorders reported that patients with a comorbid major depressive disorder diagnosis at baseline were six times more likely to remain unrecovered from restrictive anorexia nervosa 22 years later than those without depression (Franko et al., 2018). A systematic review of prevention and early intervention programs similarly highlighted the need to direct greater attention toward comorbid depressive symptoms in eating disorders: although most programs reduced eating disorder symptoms, over half were unsuccessful in reducing concurrent depressive symptoms and those that specifically targeted negative mood were no more likely to reduce depressive symptoms (Rodgers & Paxton, 2014). Thus, characterizing SE-AN through criteria that attend to severity of distress as well as duration of illness may bridge the gap across conflicting areas of evidence and thereby inform therapeutic targets.

There is also disagreement among experts about the salience of illness chronicity for treatment outcomes, with some arguing that the “severe and enduring” classification has little clinical utility. For example one recent study indicated that duration of illness, BMI and failed inpatient treatment do not predict outcome at the end of inpatient treatment (Wildes et al., 2017) and a lower powered case series (n=66) from an Italian inpatient centre failed to find differences in 12 month outcomes among those with SE-AN as defined as long duration (> 7 years) and failed previous treatment (Calugi, El Ghoch, & Dalle Grave, 2017). Another study, a case series involving outpatient cognitive behavioral therapy (n=134, with n=69 completers) concluded that duration of illness, eating disorder symptoms, and body mass index did not predict treatment outcomes, but did not indicate how many respondents were classified in the 3-, 7-, and 11-year illness duration categories (Raykos et al., 2018). Thus, it is likely that controversies regarding the

clinical utility of SE-AN classification arise in part from the variable design and quality of the studies and thus underscore the need for more research.

The present study explored the clinical utility of a definition of “severe and enduring” anorexia nervosa that considered illness duration as well as severity of psychological distress in one of the largest cohorts of patients with anorexia nervosa in the UK (Cardi et al., 2015; Cardi et al., 2019). To provide a comparison with previously reported outcomes for recipients of outpatient care, we first described changes from baseline to 12 months for individuals receiving NHS outpatient services for AN on key clinical variables (BMI, eating disorder symptoms, depression, anxiety, and stress, and work and social adjustment) and reported rates of recovery at 12 months and service usage for inpatient, daypatient, and outpatient services over the past year. To more specifically explore the clinical utility of staging classifications (such as “early stage” versus “severe and enduring” forms of illness), we assessed differences in symptomatology at baseline, changes from baseline to 12 months, rates of recovery, and service usage for individuals classified according to these schemes.

## Method

Full details of the study protocol for the SHARED trial (Cardi et al., 2015) and the primary trial outcomes (Cardi et al., 2019) are published. As intervention groups did not exhibit significant differences in eating disorder symptoms, BMI, psychological well-being, and work/social adjustment at baseline or at any of the follow-up periods, here we report on secondary data analyses from the combined sample.

### Setting and recruitment

Participants were recruited from 22 NHS adult ED outpatient services across the UK (see acknowledgements for details) between April 2015 and December 2016. The authors assert that

all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects/patients were approved by a National Research Ethics Service Committee (London Brent, approval number 14/LO/1347) and from the local research and development offices at the participating centres. Written informed consent was obtained from all patients.

## **Participants**

Participants were recruited by clinicians and clinical study officers from consecutive assessments if 1) they were aged 16 or over, 2) had a Diagnostic and Statistical Manual of Mental Disorders, 5<sup>th</sup> Edition (DSM-5) or ICD-10 diagnosis of AN or other specified feeding or eating disorder (OSFED) with features of AN and a body mass index (BMI) of 18.5 kg/m<sup>2</sup> or below. Participants were considered ineligible for the following reasons 1) insufficient knowledge of English and/or 2) severe mental or physical illness needing treatment (i.e. psychosis or diabetes mellitus). Participants completed study assessments through IESO Digital Health (<http://www.iesohealth.com>) at baseline, six weeks, six months and 12 months. Clinical teams provided additional details regarding BMI and outpatient service use at six weeks, six months and 12 months.

## **Measures**

**Demographic information and patient history.** Participants self-reported age, gender, ethnicity, years of education, employment and social status, duration of illness, time of illness onset, diagnosis and first treatment received, previous hospital admissions, psychiatric comorbidity and medication, and height and weight (which were used to calculate Body Mass

Index BMI = weight (kg) / [height (m)]<sup>2</sup>). Patient height and weight was also measured by the clinical sites and reported to the research team.

**Eating Disorder Examination Questionnaire** (Fairburn & Beglin, 1994). The EDE-Q is a 36-item self-report measure of eating disorder symptomatology. Items are scored on a six-point Likert scale, and higher scores indicate more severe eating disorder symptomatology. In the current study, we used the EDE-Q global score to assess eating disorder symptomatology (EDE-Q Cronbach's  $\alpha = 0.91$ ).

**Depression, Anxiety and Stress Scales** (Lovibond & Lovibond, 1995). The DASS-21 is a 21-item self-report measure of psychological distress over the past seven days. Items are scored on a four-point Likert scale, with higher scores indicating greater distress. The DASS-21 includes three subscales to assess symptoms of anxiety, depression, and stress, as well as an overall score to reflect general distress (DASS-total Cronbach's  $\alpha = 0.92$ ).

**Work and Social Adjustment Scale** (Marks, 1986). The WSAS is a five-item self-report measure of perceived impairment in everyday functioning due to an identified problem. The scale evaluates functioning in the following domains: work, home management, social and private leisure activities, and close relationships. Scores range from 0 to 8 for each item, with higher overall scores indicating more severe functional impairment (WSAS Cronbach's  $\alpha: 0.72$ ).

**Participant service usage.** Participants self-reported their usage of various clinical services (outpatient, daypatient, and inpatient services) related to the eating disorder over the previous 6 and 12 months. If patients did not report data on service use, we asked clinical centers to supplement this information.

## **Intervention**

Each centre delivered their usual treatment. Treatment in NHS clinics follows the NICE guidelines and quality standards (NICE, 2017), which recommend outpatient care in the first instance with transfer to day/inpatient if and when the level of risk is high. The form of treatment is determined only by clinical decision of level of need and is free at the point of delivery. The group randomised to receive the adjunctive intervention received early phase 6-week online chat guidance delivered via a digital platform along with psychoeducational material supplemented with recovery narratives (Cardi et al., 2015). The intervention was designed to enhance motivation and decrease engagement with the psychopathology of anorexia nervosa and facilitate the development of a recovery identity.

## **Data Analyses**

All analyses were conducted in SPSS Version 26.0. We used multiple imputation for missing data at the 6-month and 12-month assessments, and conducted paired t-tests to assess changes on key clinical indicators (BMI, EDE-Q, DASS, WSAS) from baseline to the follow-up assessments for the full sample. We conducted frequency analyses to assess service usage related to the eating disorder (past hospitalization assessed at baseline, and use of inpatient, day patient, and outpatient services over the past 6 months and 12 months) and recovery. We defined “recovery” as a combination of BMI ( $\geq 18.5$ ) and eating disorder symptoms (EDE-Q 1 standard deviation above the nonclinical mean, or EDE-Q  $< 2.77$ ; (Mond, Hay, Rodgers, Owen, & Beumont, 2004)) following past research (Couturier & Lock, 2006).

For our exploratory analyses comparing baseline functioning and outcomes for respondents in the “early stage” vs. “severe and enduring” illness, we defined “early stage” as illness duration less than 3 years (Brown et al., 2018; Russell et al., 1987). Past studies on SE-AN typically rely on duration, but not severity, criteria in defining a “severe and enduring”

group, and although related, severity is not equivalent to illness duration. For instance, among our respondents, duration of illness was correlated with one indicator of illness severity, BMI ( $r = -.25, p = .001$ ), but correlations with other clinical indicators at baseline (such as EDE-Q, DASS, and WSAS) were small and non-significant. Moreover, the revised cognitive interpersonal model posits that secondary neuroprogressive changes associated with high stress, anhedonia, and elevated fears are relevant for clinical functioning and outcomes in AN (Treasure et al., under review). Thus, a composite variable comprising severity and duration indicators likely captures unique variance above and beyond duration of illness alone. We evaluated several options for defining SE-AN through a composite of duration and BMI, duration and EDE-Q, duration and WSAS, and duration and DASS, and these comparisons are reported in the supplementary materials. However, we chose to define SE-AN in the current investigation as a combination of severity of psychological distress (DASS-total  $\geq 60$ ; (Beaufort, De Weert-Van Oene, Buwalda, De Leeuw, & Goudriaan, 2017) and duration of illness ( $\geq 7$  years; (Robinson, 2009; Touyz et al., 2013) due to the centrality of psychological distress for the phenomenology of disordered eating.

We then conducted a chi-square analysis comparing groups on lifetime and past year usage of intensive services (day/inpatient care), followed by independent samples t-tests comparing “early stage” vs. “severe and enduring” groups on baseline functioning (EDE-Q, BMI, WSAS). Finally, we conducted mixed repeated measures ANOVAs to compare changes from baseline to 12 months across “early stage” and “severe and enduring” classification groups on BMI, EDE-Q, and WSAS.

## Results

### Participant characteristics

One-hundred eighty-seven participants completed the baseline assessment (see Table 1 for demographic and descriptive information). There was large variation in the clinical characteristics. Many had a long duration of illness ( $M = 7.76$  years;  $SD = 8.91$  years) with a 5-year gap between self-recognized eating disorder symptoms and the start of treatment and their BMI had fallen by  $6.3 \text{ kg/m}^2$ . Over a quarter had previously received inpatient care and reported psychiatric co-morbidity, and 44.3% were receiving psychiatric medication. Both eating disorder psychopathology (EDE-Q) and levels of depression, anxiety, and stress (DASS) were elevated and psychosocial function was impaired (WSAS).

#### **Adherence to the follow up protocol**

For questionnaire measures (EDE-Q, DASS, WSAS) there was 75.4% completion at 6 months and 62.6% at 12 months. For service usage, 74.9% reported on their service usage at 6 months and 61.5% at 12 months. We obtained some missing data (weight and service use) from clinical sites, resulting in BMI data for 70% of participants at 6 and 12 months.

#### **Clinical outcomes, service use, and rates of “recovery” at follow-up**

Paired t-tests using multiple imputation data indicated small improvements from baseline to 6 months in distress (DASS Hedge’s  $g = 0.28$ ) and work and social adjustment (WSAS Hedge’s  $g = 0.30$ ), and moderate improvements in BMI (Hedge’s  $g = 0.57$ ) and eating disorder symptoms (EDE-Q Hedge’s  $g = 0.54$ ) (see Table 2). Small to moderate improvements on these outcomes were maintained at 12 months, with the only exception of BMI, which was associated with a larger effect size at the 12 month assessment (Hedge’s  $g = 0.85$ ).

Among those who participated in the 12-month assessment, frequency analyses indicated that a large proportion remained in outpatient care (86/115; 74.8%). Data from the 6-month and 12-month assessment periods indicated that over a third of respondents (44/123; 35.8%) accessed



intensive care (i.e., inpatient or daypatient services) at some point over the past year. Among those who continued with follow-up assessments at 12 months ( $n = 123$ ), 23.6% of respondents met BMI and EDE-Q criteria for recovery<sup>1</sup>.

#### **Exploratory analyses comparing clinical outcomes for “early stage” vs. “severe and enduring” respondents**

**Service Usage.** A chi-square analysis of independence compared “early stage” and “severe and enduring” respondents in their usage of intensive services (inpatient/daypatient) either at baseline or at follow-up assessments. Results indicate that SE-AN respondents were more likely to have received (29/35; 82.9%) intensive care at some point as compared to “early stage” respondents (18/39 = 46.2%),  $\chi^2(1) = 10.72, p = .001$ .

**Baseline differences.** A series of independent samples t-tests comparing the “early stage” and SE-AN groups on key clinical indicators at baseline indicated moderate sized, significant group differences for EDE-Q and WSAS, and small and nonsignificant differences for BMI (see Table 3).

**12 month outcomes.** Mixed repeated measures ANOVAs compared changes from baseline to 12-months for BMI, EDE-Q, and WSAS by “early stage” versus “severe and enduring” classification. Results indicated main effects for time and group, with improvements over time on all three markers, but poorer functioning on all three markers for the SE-AN group (see Figures 1-3). Moreover, there was a significant time x illness group interaction for WSAS, indicating relatively less improvement on this indicator over time for the SE-AN group (see Table 3). There was a trend toward significance for the time x illness group interactions for BMI

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<sup>1</sup> Given different published EDE-Q norms for community women, we also tested an alternate criterion for “recovery” ( $EDE-Q < 1.79$  per Aardoom et al., 2012). Based on these criteria ( $EDE-Q < 1.79$  and  $BMI \geq 18.5$ ), 13.8% of respondents met the threshold for recovery at 12 months.

and EDE-Q ( $p = .06$ ) and examination of the box plots suggested a similar pattern with lower rates of improvement over time for the SE-AN group.

### **Exploratory analyses evaluating clinical outcomes based on varying SE-AN classification schemes**

A series of exploratory independent samples t-tests comparing non-SE-AN and SE-AN respondents by varying classification schemes (i.e., duration combined with either high DASS, low BMI, high EDE-Q, or high WSAS) suggested several differences in clinical functioning at baseline across groups with SE-AN respondents exhibiting poorer clinical functioning (medium to large effect sizes) than non-SE-AN respondents at baseline. However, results varied as a function of the classification scheme and the nature of the outcome variable (see Table S1). We then conducted a series of exploratory mixed repeated measures ANOVAs comparing changes from baseline to 12 months on clinical indicators for the SE-AN vs. non-SE-AN respondents. In general, results indicated improvements over time, and differences in outcomes based on classification group, but differences in the trajectory of change over time by classification group were nonsignificant when SE-AN was defined by WSAS, EDE-Q, and in most cases, BMI. However, results indicated significant interaction effects when SE-AN was defined by DASS, such that the rates of improvement over time for BMI, EDE-Q, and WSAS were smaller for the SE-AN than non-SE-AN respondents.

## **Discussion**

The current study reported clinical outcomes, service use, and differences by staging classification for people receiving outpatient care for anorexia nervosa in the UK. Overall, we found large to moderate improvements in BMI, eating disorder symptoms and moderate changes in mood symptoms, and work and social adjustment at 12 months, which is consistent with

1 previously reported improvements in BMI among recipients of adult outpatient treatment (Zeeck  
2 et al., 2018). However, previously published rates of accessing intensive services are more  
3 mixed, with estimates ranging from 11.9%-15.6% in a UK trial (Schmidt et al., 2015) to 23%-  
4 41% in a German trial (Zipfel et al., 2014), and our finding that 35.8% reported transitioning to a  
5 higher intensity of treatment (in/day patient care) during the year fall within the higher end of the  
6 spectrum. Among those who continued with follow-up assessments at 12 months ( $n = 123$ ), less  
7 than a quarter (23.6%) of respondents met criteria for recovery as defined by body mass index  
8 and eating disorder symptoms. These lower than desirable levels of improvement are consistent  
9 with results from a recent systematic review and meta-analysis, which reported high levels of  
10 residual symptoms even among patients with AN who were considered remitted or recovered  
11 (Tomba, Tecuta, Crocetti, Squarcio, & Tomei, 2019).

12       Our major objective was to explore the clinical utility of classification schemes for  
13 anorexia nervosa based on markers of psychological distress and illness duration. Approximately  
14 36% (60/166) of our respondents were classified as “early stage” and 25% (41/166) were  
15 classified as “severe and enduring.” Patients in the SE-AN group reported more lifetime  
16 hospitalizations and worse eating disorder symptoms, psychological functioning and work and  
17 social wellbeing compared to patients with shorter illness duration. Patients in the SE-AN group  
18 also reported less symptomatic changes over time compared to the “early phase” group,  
19 especially in relation to work and social adjustment. Exploratory results also suggest less  
20 improvement in eating disorder symptomatology, work and social adjustment, and BMI over  
21 time for those classified as SE-AN as compared to those identified as non-SE-AN. These data  
22 support the clinical utility of SE-AN classification based on the previously established threshold  
23 of 7 years of illness with the addition of emotional distress as an index of severity.

1           There is very little evidence on the specific treatment of individuals classified as having  
2   “severe and enduring” anorexia nervosa apart from a few investigations (Andries, Frystyk,  
3   Flyvbjerg, & Støving, 2014; Calugi et al., 2017; Dalton et al., 2018; Lipsman et al., 2017; Touyz  
4   et al., 2013). Nevertheless, many studies in adults include a large number of patients that fall into  
5   this subgroup and suggest lower response to treatment: for instance, studies testing olanzapine  
6   (Attia et al., 2019) and dronabinol (Andries et al., 2014) report small improvements in weight  
7   gain but little change in other domains. Thus, there is an urgent need for research on  
8   interventions targeting individuals with a chronic course of illness (Wonderlich et al., 2012).

### 9   **Strengths and limitations**

10           The present study reported on service use and clinical outcomes for the largest, most  
11   representative sample of patients receiving outpatient services for AN in the UK over a 12-month  
12   follow-up period. Attrition from protocol follow-up (30%) was within the range reported in a  
13   systematic review of previous studies in anorexia nervosa (DeJong, Broadbent, & Schmidt,  
14   2012) and therefore we used multiple imputation for missing data where possible. A strength of  
15   the study is that it fulfils proposed benchmark criteria for AN intervention research including  
16   reporting on separate physiological (BMI), cognitive/affective (EDE-Q, DASS) and  
17   social/functional (WSAS) outcome indicators, in addition to providing details about service use  
18   over the course of a follow-up period (Murray, Loeb, & Le Grange, 2018). Moreover, given  
19   recent scrutiny of bias in anorexia nervosa treatment outcome research (Murray et al., 2019), we  
20   are pleased to report that we participated in pre-registration of the protocol (Cardi et al., 2015),  
21   completed the trial as proposed, published the primary outcomes (Cardi et al., 2019), and will be  
22   making study materials and data publicly available to facilitate replication and extension.  
23   However, our analyses comparing “early stage” and “SE-AN” responses involved modest

1 samples, given the stringent criteria used to define these groups, and we did not statistically  
2 control for our multiple comparisons due to the exploratory nature of our analyses. Thus, present  
3 findings are limited and require further replication and extension in larger samples of participants  
4 receiving outpatient care for anorexia nervosa.

### 5 **Clinical implications**

6 The NICE guidelines (NICE, 2004, 2017) recommend that the care pathway for anorexia  
7 nervosa should begin with outpatient treatment, however, there is likely a great deal of service  
8 variability across treatment centers and patients may have been assigned to waiting lists  
9 following the assessment period. In our study, there were small to large improvements across  
10 clinical indicators in this naturalistic setting, but less than a quarter had reached the criteria for  
11 “recovery” at 12 months. Over a third of patients were transferred to day/inpatient care because  
12 of medical and or psychiatric risk, and over three quarters of patients remained in treatment at 12  
13 months. These data offer a point of comparison for outpatient care outcomes, whilst highlighting  
14 the need to more closely scrutinize the nature of treatment as usual across care settings, including  
15 an assessment of their ability to provide care without delay.

16 There remains uncertainty in the literature as to whether categorization by “early stage”  
17 vs. “severe and enduring” has implications for treatment and services. Our findings lend support  
18 for a model where longer duration of illness and poorer psychological wellbeing might require  
19 more specific treatment efforts. For instance, individuals with SE-AN may benefit from  
20 neuromodulation interventions targeting treatment-resistant depression, such as deep brain  
21 stimulation and repetitive transcranial magnetic stimulation, or from pharmacological approaches  
22 such as ketamine and psilocybin (Treasure et al., under review). Indeed, our investigation  
23 highlights the salience of distress as an indicator of illness severity, thus, directing greater

1 attention toward the role of such distress could clarify useful mechanisms for additional  
2 intervention and suggest possibilities for a combined approach targeting both mood and eating  
3 disorder symptomatology. However, we acknowledge that staging efforts should consider  
4 associated risks for increased stigmatization and pursue strategies to mitigate the potential for  
5 such harm.

6 Although some clinical practice guidelines have been developed to address the needs of  
7 patients with SE-AN (e.g. guidelines from the Royal Australian and New Zealand College of  
8 Psychiatrists (Hay et al., 2014), the Royal College of Psychiatrists' MARSIPAN (Robinson &  
9 Rhys Jones, 2018), and The British Columbia Ministry of Health (Geller, Goodrich, Chan,  
10 Cockell, & Srikaneswaran, n.d.)), we believe that further work is needed to characterize the  
11 clinical needs of this patient group and to implement a combined approach that targets both  
12 mood and eating disorder symptoms.

### 13 **Conclusion**

14 We provide evidence of low “recovery” rates (23%) and relatively high rates of  
15 admission to more intense forms of treatment (36%) among a large UK-based population of  
16 patients with anorexia nervosa assessed for outpatient treatment. This is despite overall large  
17 improvements in BMI and moderate improvements in eating disorder psychopathology.  
18 Moreover, treatment gains were more modest for patients with a severe and enduring form of  
19 illness characterized by longer duration and worse psychological wellbeing. We suggest that  
20 using treatment strategies to provide rapid relief of symptoms of low mood and greater support  
21 with psychosocial functioning may be useful to enhance standard care for adult anorexia nervosa.

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